REMARKS

Applicant encloses an appendix that shows the changes made to claims 38, 39, 42, 43, and 46 by the current amendment. New claims 47-56 have been added. Following entry of this amendment, claims 38-56 are pending and under consideration in the application.

Support for the recitation of "monoclonal" in claims 38 and 39 can be found in the specification, e.g., at page 11, lines 6-9. Claims 38 and 39 have been amended to recite "binds a polypeptide consisting of..." rather than "binds a polypeptide comprising." This amendment merely clarifies that the claimed antibodies bind to an epitope within the polypeptide sequence recited in the claim. Claims 38, 39, and 42 have been amended to remove the recitation of "specifically." Claims 43 and 46 have been amended to remove the recitation of "a therapeutically effective amount of."

Support for new claim 47 can be found in the specification, e.g., at page 11, lines 3-5, and at page 5, lines 27-28. Support for new claims 48, 49, 53, and 54 can be found in the specification, e.g., at page 11, lines 6-9. Support for new claims 50 and 55 can be found in the specification, e.g., at page 13, lines 23-24. Support for new claims 51 and 56 can be found in the specification, e.g., at page 13, lines 11-14. Support for new claim 52 can be found in the specification, e.g., at page 11, lines 3-5, and at page 22, lines 9-12.

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Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 38-46 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Action at page 3, item no. 6. The Examiner alleged that

"[t]he phrase 'specifically binds' renders the bounds of the claims unascertainable because it is used in the art in a relative way to denote varying degrees of specificity." *Id.*

Solely to expedite prosecution and without acquiescing to the rejection, applicants have amended claims 38, 39, and 42 to remove the recitation of "specifically." Claim 38 recites

> [a] monoclonal antibody or fragment thereof that binds a polypeptide consisting of an amino acid sequence selected from:
> (a) amino acids 1 to 524 of SEQ ID NO: 11,
> (b) amino acids 1 to 547 of SEQ ID NO: 13, and
> (c) amino acids 1 to 547 of SEQ ID NO: 15.

Claims 40, 41, and 46 depend from claim 38. Claim 39 recites "[a] monoclonal antibody or fragment thereof of claim 38, wherein the antibody or fragment thereof binds a polypeptide consisting of amino acids 1 to 524 of SEQ ID NO: 11." Claim 42 recites "[a] monoclonal antibody or fragment thereof that binds a polypeptide comprising an amino acid sequence as set forth in SEQ ID NO: 11." Claims 43-45 depend from claim 42.

Applicants assert that the amendments to claims 38, 39, and 42 render the rejection moot. Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 43 and 46 under 35 U.S.C. § 112, first paragraph, as allegedly "containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains...to make and/or use the invention." Action at page 4, item no. 8. The Examiner alleged that "the specification does [*sic*] provide sufficient guidance as to what the antibody is

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therapeutically effective for; and neither can such a use be reasonably inferred from the prior art." *Id.* Applicants assume that the Examiner intended to assert that "the specification does *not* provide sufficient guidance as to what the antibody is therapeutically effective for..." and will respond to the rejection accordingly. The Examiner further alleged that "there does not appear to be evidence of a correlation between interfering with Hek5 by binding and corresponding abrogation of cancer." *Id.*

Applicants assert that evidence of a correlation between interfering with Hek5 by binding and corresponding abrogation of cancer is not necessary for the claimed antibodies to be therapeutically effective. As discussed in the Amendment and Response filed January 25, 2002, overexpression of HEK5 is correlated, e.g., with gastric cancer. See pages 4 and 5 of that Amendment. Applicants assert that one skilled in the art would recognize that this correlation suggests that the antibodies may be used, e.g., to specifically target anticancer agents to cancer cells. Such uses do not necessarily require that binding to the antigen alone correlates with abrogation of cancer.

Solely to expedite prosecution and without acquiescing to the rejection, claim 43 has been amended to recite "[a] pharmaceutical composition comprising an antibody of claim 42 in a mixture with a pharmaceutically acceptable adjuvant, carrier, solubilizer, or diluent" and claim 46 has been amended to recite "[a] pharmaceutical composition comprising an antibody of claim 38 in a mixture with a pharmaceutically acceptable adjuvant, carrier, solubilizer, or diluent." Thus, the rejected claims no longer recite "a therapeutically effective amount" and the rejection is moot.

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Applicants respectfully request reconsideration and withdrawal of the rejection of claims 43 and 46 under 35 U.S.C. § 112, first paragraph.

Rejection under 35 U.S.C. § 102(b)

The Examiner rejected claims 38 and 39 under 35 U.S.C. § 102(b), as allegedly being anticipated by Pasquale. Action at page 5, item no. 10. The Examiner alleged that "absent evidence to the contrary, the polyclonal antibodies disclosed by Pasquale are expected to specifically bind to the polypeptide of SEQ ID NO: 11." *Id.*

Solely to expedite prosecution and without acquiescing to the rejection, claim 38 has been amended to recite

> [a] monoclonal antibody or fragment thereof that binds a polypeptide consisting of an amino acid sequence selected from:
> (a) amino acids 1 to 524 of SEQ ID NO: 11,
> (b) amino acids 1 to 547 of SEQ ID NO: 13, and
> (c) amino acids 1 to 547 of SEQ ID NO: 15.

Also, solely to expedite prosecution and without acquiescing to the rejection, claim 39 has been amended to recite "[a] monoclonal antibody or fragment thereof of claim 38, wherein the antibody or fragment thereof binds a polypeptide consisting of amino acids 1 to 524 of SEQ ID NO: 11." Applicants will also address the rejection with respect to new claims 47 and 52, which recite "[a]n antibody or fragment thereof which is raised against at least a portion of a polypeptide comprising SEQ ID NO: 11" and "[a]n antibody or fragment thereof which is raised against at least a portion of amino acids 1 to 524 of SEQ ID NO: 11," respectively.

Applicants note that in order to anticipate a claim, a reference must teach every element of that claim. MPEP § 2131. Applicants assert that Pasquale does not teach a

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monoclonal antibody or fragment thereof. Furthermore, the claimed monoclonal antibodies bind to a single epitope, while the polyclonal antibodies discussed by Pasquale bind to many epitopes. Therefore, Pasquale cannot anticipate claim 38. Claim 39 is dependent from claim 38 and includes every element of claim 38. Pasquale therefore also cannot anticipate claim 39.

The Examiner proposed that a claim that recites "[a]n isolated antibody or fragment thereof which is raised against and specifically binds to a polypeptide comprising SEQ ID NO: 11" would overcome the rejection. Action at page 6. Claim 47 recites "[a]n antibody or fragment thereof which is raised against at least a portion of a polypeptide comprising SEQ ID NO: 11." Claim 47 therefore recites antibodies raised against at least a portion of SEQ ID NO: 11, which is the sequence of the human protein HEK5. In contrast, Pasquale only discusses antibodies raised against the chicken protein CEK5. Pasquale does not teach antibodies raised against HEK5. Applicants therefore assert that Pasquale does not teach every element of claim 47 and thus cannot anticipate that claim.

The Examiner also proposed that a claim that recites "[a]n isolated antibody or fragment thereof which is raised against and specifically binds to amino acids 1 to 524 of SEQ ID NO: 11" would overcome the rejection. *Id.* Claim 52 recites "[a]n antibody or fragment thereof which is raised against at least a portion of amino acids 1 to 524 of SEQ ID NO: 11." Claim 52 therefore recites antibodies raised against at least a portion of amino acids 1 to 524 of the human protein HEK5. In contrast, Pasquale only discusses antibodies raised against the chicken protein CEK5. As discussed above, Pasquale does not teach antibodies raised against HEK5. Applicants therefore assert

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that Pasquale does not teach every element of claim 52 and thus can not anticipate that claim.

Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b).

Rejection under 35 U.S.C. § 103(a)

The Examiner rejected claims 40-42, 44, and 45 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Pasquale in view of U.S. Patent No. 4,816,567 (the '567 patent). Action at page 7, item no. 12. The Examiner alleged that "it would be obvious to one of ordinary skill in the art at the time the invention was made, with reasonable expectation of success, to make a monoclonal, chimeric, or CDR grafted antibodies according to [the '567 patent] when practicing the invention of Pasquale EB." *Id.*

Claims 40 and 41 are dependent from claim 38 and recite "[t]he antibody or fragment thereof of claim 38, which is a chimeric antibody" and "[t]he antibody or fragment thereof of claim 38, which is a CDR-grafted antibody," respectively. Claim 38 recites

> [a] monoclonal antibody or fragment thereof that binds a polypeptide consisting of an amino acid sequence selected from:
> (a) amino acids 1 to 524 of SEQ ID NO: 11,
> (b) amino acids 1 to 547 of SEQ ID NO: 13, and
> (c) amino acids 1 to 547 of SEQ ID NO: 15.

Claim 42 recites "[a] monoclonal antibody or fragment thereof that binds a polypeptide comprising an amino acid sequence as set forth in SEQ ID NO: 11." Claims 44 and 45 are dependent from claim 42 and recite a chimeric antibody and a CDR-grafted

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antibody, respectively. Applicants will also address the rejection with respect to new claims 48-50, which are dependent from claim 47, and new claims 53-55, which are dependent from claim 52. Claims 47 and 52 recite "[a]n antibody or fragment thereof which is raised against at least a portion of a polypeptide comprising SEQ ID NO: 11" and "[a]n antibody or fragment thereof which is raised against at least a portion of amino acids 1 to 524 of SEQ ID NO: 11," respectively. Claims 48 and 53 recite a monoclonal antibody, claims 49 and 54 recite a chimeric antibody, and claims 50 and 55 recite a CDR-grafted antibody.

Applicants assert that Pasquale does not teach and would not have suggested an antibody or fragment thereof that binds a polypeptide as set forth in SEQ ID NO: 11. Pasquale also does not teach and would not have suggested an antibody or fragment thereof that binds a polypeptide consisting of amino acids 1 to 524 of SEQ ID NO: 11. SEQ ID NO: 11 shows the sequence of the human protein HEK5. In contrast, Pasquale only discusses the chicken protein CEK5. Applicants assert that Pasquale does not teach and would not have suggested the human protein HEK5 or antibodies that bind to the human protein HEK5. The '567 patent fails to remedy the deficiencies of Pasquale. Therefore applicants assert that the combination of Pasquale and the '567 patent would have failed to suggest monoclonal antibodies or fragments according to claims 40-42, 44, and 45.

Moreover, for the reasons discussed above for the rejection under 35 U.S.C. § 102(b), applicants assert that Pasquale does not teach antibodies or fragments thereof that are raised against at least a portion of a polypeptide comprising SEQ ID NO: 11. Pasquale also does not teach antibodies or fragments thereof that are raised

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against at least a portion of amino acids 1 to 524 of SEQ ID NO: 11. Moreover, the Examiner has not established that Pasquale would have suggested such antibodies or fragments. The '567 patent fails to remedy those defects.

Thus, the Examiner has failed to establish that the combination of Pasquale and the '567 patent would have rendered obvious claims 40-42, 44, 45, 48-50, and 53-55. Moreover, applicant need not address the Examiner's contentions concerning the combination of Pasquale and the '567 patent with respect to other limitations of certain dependent claims. By not addressing those contentions, applicant in no way acquiesces to those contentions.

Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) over Pasquale in view of the '567 patent.

The Examiner rejected claims 38-42, 44 and 45 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Iwase et al., Biochem. Biophys. Res Comm. 194(2) 698-705, 1993 (Iwase) in view of the '567 patent. Action at page 8, item no. 13. The Examiner alleged that "[a]pplicant asserts (Paper 14) that the polypeptide taught by Iwase et al., is the polypeptide of the instant SEQ ID NO: 11." *Id.* The Examiner further alleged that "it would have been obvious to one of ordinary skill in the art, at the time the invention was made, to make monoclonal antibodies, CDR grafted and otherwise chimeric antibodies to the polypeptide taught by Iwase et al." *Id.* Applicant respectfully traverses.

Applicants never asserted that the H1 polypeptide taught by Iwase is identical to SEQ ID NO: 11, as the Examiner suggests. Rather, H1 appears to be similar to amino

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acids 624 to 970 of SEQ ID NO: 11, although H1 contains at least three amino acid differences relative to that region of SEQ ID NO: 11. As discussed above, claim 38 recites a monoclonal antibody or fragment thereof that binds to amino acids 1 to 524 of SEQ ID NO: 11. Claim 52 recites an antibody or fragment thereof raised against at least a portion of amino acids 1 to 524 of SEQ ID NO: 11.

Iwase does not discuss amino acids 1 to 524 of SEQ ID NO: 11. Thus, applicants assert that Iwase does not teach and would not have suggested an antibody that binds to amino acids 1 to 524 of SEQ ID NO: 11. Iwase also does not teach and would not have suggested an antibody or fragment thereof that was raised against at least a portion of amino acids 1 to 524 of SEQ ID NO: 11. The '567 patent does not remedy those deficiencies. Applicants therefore assert that the combination of Iwase and the '567 patent would not have rendered claims 38 and 52 obvious. Claims 39-41 are dependent from claim 38 and claims 53-55 are dependent form claim 52. Thus, those claims would not have been obvious over the combination of Iwase and the '567 patent.

Claim 42 recites a "monoclonal antibody or fragment thereof that binds a polypeptide comprising an amino acid sequence as set forth in SEQ ID NO: 11." Claims 44 and 45 depend from claim 42. Claim 47 recites an antibody or fragment thereof that was raised against at least a portion of a polypeptide comprising SEQ ID NO: 11. Claims 48-50 are dependent from claim 47. Applicants assert that Iwase does not teach and would not have suggested an amino acid sequence as set forth in SEQ ID NO: 11. SEQ ID NO: 11 is a 970 amino acid sequence. In contrast, Iwase only discusses a sequence of about 346 amino acids. Therefore, applicants assert that

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Iwase does not teach and would not have suggested an antibody or fragment thereof that binds a polypeptide comprising an amino acid sequence as set forth in SEQ ID NO: 11. Iwase also does not teach and would not have suggested an antibody or fragment thereof that was raised against at least a portion of a polypeptide comprising SEQ ID NO: 11. The '567 patent does not remedy those deficiencies.

Thus, the Examiner has failed to establish that the combination of Iwase and the '567 patent would have rendered obvious claims 38-42, 44, and 45. Moreover, applicant need not address the Examiner's contentions concerning the combination of Iwase and the '567 patent with respect to other limitations of certain dependent claims. By not addressing those contentions, applicant in no way acquiesces to those contentions.

Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) over Iwase in view of the '567 patent.

Applicants respectfully assert that the present application is in condition for allowance and request that the Examiner issue a timely Notice of Allowance. If the Examiner does not consider the application to be allowable, the undersigned requests that, prior to taking action, the Examiner call her at (650) 849-6656 to set up an interview.

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Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

Dated: August 30, 2002

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APPENDIX TO AMENDMENT AND RESPONSE

Version with Markings to Show Changes Made

IN THE CLAIMS:

Please amend claims 38, 39, 43, and 46 to read as follows:

38. (Amended) [An] A monoclonal antibody or fragment thereof that [specifically] binds a polypeptide [comprising any of] consisting of an amino acid sequence selected from:

(a) amino acids 1 to 524 of SEQ ID NO: 11,

(b) amino acids 1 to 547 of SEQ ID NO: 13, [or] and

(c) amino acids 1 to 547 of SEQ ID NO: 15.

39. (Amended) [An] A monoclonal antibody or fragment thereof of claim 38, wherein the antibody or fragment thereof [specifically] binds a polypeptide [comprising] consisting of amino acids 1 to 524 of SEQ ID NO: 11.

42. (Amended) A monoclonal antibody or fragment thereof that [specifically] binds a polypeptide comprising an amino acid sequence as set forth in SEQ ID NO: 11.

43. (Amended) A pharmaceutical composition comprising [a therapeutically effective amount of] an antibody of claim 42 in a mixture with a pharmaceutically acceptable adjuvant, carrier, solubilizer, or diluent.

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46. (Amended) A pharmaceutical composition comprising [a therapeutically effective amount of] an antibody of claim 38 in a mixture with a pharmaceutically acceptable adjuvant, carrier, solubilizer, or diluent.

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